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HODGSON RUSS LLP
THE GUARANTY BUILDING
140 PEARL STREET
SUITE 100
BUFFALO, NY 14202-4040

EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,498	ANSORGE ET AL.	
	Examiner	Art Unit	
	JULIE HA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *1-4,6-12 and 15-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restriction filed on January 17, 2008 is acknowledged. Claims 1-17 are pending in this application.

Restriction

1. Applicant's election of Group II (claims 5 and 13-14) and species (Lys[Z(NO_2)thiazolidide) as DP IV inhibitor, actinonin as the APN inhibitor, benign fibrotic and sclerotic diseases as the species of diseases, oral as the systemic application, and creams as the topical application in the reply filed on January 17, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. The Restriction requirement is deemed proper and made FINAL. Claims 1-4, 6-12 and 15-17 have been withdrawn from further consideration, pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 5 and 13-14 are examined on the merits in this office action.

Objections-Minor Informalities

3. The title is objected to because the title is too long. The title is limited to 2-7 words maximum (see MPEP 601). A new title is required that is clearly indicative of the invention to which the claims are directed.

4. The specification is objected to because there seems to be inconsistency with the spelling of "Actinonin". Throughout the specification, "actinonin" is spelled "actinonin". However, in Figure 3, "actinonin" is spelled "Actinonine" in the description of Figure 3, and in the legend (boxed), it is spelled "actinonin". Please correct the spelling so that the spelling is consistent throughout the specification.

5. The specification is objected to because the spelling of "Figure" appears to be missing an "e" from Figures 1-3. For example, "Figure 1" is spelled out "Figur 1". Applicant is advised to correct the spelling errors.

Rejection-35 U.S.C. 112, 2nd

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 5 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Regarding claims 5 and 14, the phrases "preferably", "in particular", and "for example" renders the claims indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). These phrases make it unclear as to whether scopes of the claims are to be limited to the more specific embodiments recited in the claims.

9. Claim 14 recites, "said inhibitors being selected from inhibitors of CPIV and particularly preferable from Xaa-Pro-dipeptides (Xaa = a-amino acid or side chain-

protected derivative), corresponding derivatives, more preferably dipeptide phosphonic acid diaryl esters...corresponding derivatives and their salts...corresponding derivatives and their salts...TSL derivatives..." The phrases "derivatives", "side chain protected derivative" and "their derivatives serve as the amide structure" are unclear. It is unclear what types of modifications constitute the derivatives. For example, there are chemical, physical, and enzymatic modifications that can occur to the chemical species, such as a pH change or H-bonding or bond cleavage. Therefore, it is unclear what types of modifications would encompass the derivatives. Furthermore, it is unclear what would constitute a side chain protected derivative, when L-proline, L-tryptophan, cyclic amines would not have side chains available for protection. Additionally, it is unclear what is meant by "their derivatives serve as the amide structure", since amide structure has the following structure: 

. It is unclear what modifications would constitute the derivatives of amide structure.

Rejection-35 U.S.C. 112, 1st

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 5 and 13-14 are rejected are under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in

the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature or the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (5) the breadth of the claims:

The claims are drawn to a method of utilizing inhibitors of dipeptidyl peptidase IV (DP IV) and of enzymes having the same or a similar substrate specificity (DP IV analogous enzyme activity) separately or in any combination with inhibitors of alanyl aminopeptidase (APN) and or enzymes having the same or a similar substrate specificity (APN analogous enzyme activity) for a prevention and therapy of dermatologic diseases. The claims do not indicate the patient population. The claims are broadly drawn to methods of treating or preventing dermatologic diseases, such as

benign fibrotic and sclerotic diseases (hypertrophic scars and keloids) in a host comprising administration of inhibitors of dipeptidyl peptidase IV (DPIV) or DPIV-analog or/and inhibitors of alanyl aminopeptidase (Aminopeptidase N, APN) or APN-analogs.

(2) The state of the prior art and (4) the predictability or unpredictability of the art::

The Merck manual indicates that keloids are smooth overgrowth of fibroblastic tissue that arise in an area of injury or, occasionally, spontaneously. The Merck manual indicates that keloidal scar tissue always extends beyond the area of original injury. Furthermore, the Merck manual indicates that diagnosis is clinical and treatment is often ineffective. Surgical or laser excision may debulk lesions, but they often recur (see Merck manual, "Keloids").

Berman B (http://emedicine.com/derm/topic205.htm) indicates that keloids are the result of an overgrowth of dense fibrous tissue that usually develops after healing of a skin injury. The tissue extends beyond the borders of the original wound, does not regress spontaneously, and tends to recur after excision. Hypertrophic scars are erythematous, pruritic, raised fibrous lesions that typically do not expand beyond the boundaries of the initial boundaries of the initial injury and may undergo partial spontaneous resolution, and are common after thermal injuries and other injuries that involve the deep dermis (see Background). The reference indicates that as scar matures, the tensile strength of the scar improves as a result of progressive cross-linking collagen fibers. Furthermore, the reference indicates that Kischer and Brody declared the collagen nodule to be the identifying structural unit of hypertrophic scars

and keloids; the nodule, which is absent from mature scars, contains a high density of fibroblasts and unidirectional collagen fibrils in a highly organized and distinct orientation. The reference indicates that the most consistent difference between hypertrophic scar and keloids is the presence of broad, dull, pink bundles of collagen in keloids, which are not present in hypertrophic scars (see Pathophysiology). Furthermore, the reference indicates that keloids and hypertrophic scars do not usually cause symptoms, but they may be tender, painful, or pruritic or they may cause a burning sensation (see History). The reference indicates that the exact mechanisms of keloids and hypertrophic scar pathogenesis is not known, and no specific gene or set of genes has been identified; the presence of foreign material, infection, hematoma, or increased skin tension can also lead to keloid or hypertrophic scar formation in susceptible individuals (see Causes). Further, formation of collagen in keloids and hypertrophic scars in the inflammatory stage takes much longer than usual in healing wounds. Collagen fibers in granulation tissue are arranged in a whorled pattern; in keloids, the nodules demonstrate thick, hyalinized bands in the central portion of the nodule (see Histologic Findings). The reference indicates that "prevention is key", and indicates that preventive measures are: 1) avoid performing nonessential cosmetic surgery, 2) close all surgical wounds with minimal tension, 3) incisions should not cross joint spaces, and 4) avoid making midchest incisions (see Medical care). The reference describes different types of treatments and therapies (see Medical care and Surgical care).

Pierson JC (http://emedicine.com/derm/topic96.htm, enclosed) indicates dermatofibroma (DF) is a common cutaneous nodule of unknown etiology that occurs more often in women. The lesions frequently develop on the extremities and are usually asymptomatic, although pruritus and tenderness are not uncommon (see Background). Further, the reference indicates that the precise mechanism for the development of DF is unknown. DF seems more likely to be a neoplastic process due to the persistent nature of the lesion and the demonstration that it is a clonal proliferative growth; transforming growth factor-beta (TNF-β) might be a trigger of the fibrosis seen in DF (see Pathophysiology). The reference indicates that the bulk of the "tumor" is within the mid dermis where no capsule is present and the periphery of the lesion blends with the surrounding tissue. Whorling fascicles of a spindle cell proliferation with excessive collagen deposition are characteristic (see Histologic Findings). The reference indicates intralesional steroid injections or surgical care as types of treatments available for DF (see Medical Care and Surgical Care).

Young et al (US Patent No. 5,827,735) teaches that degradation of collagen is as important as collagen production and lack of collagen degradation can result in excessive deposition, i.e., keloid, hypertrophic scar, or hepatic fibrosis (see column 5, lines 11-18). Furthermore, the reference teaches that it is important to note that collagen synthesis has nothing to do with the gain in wound tensile strength. Tensile strength results from collagen cross-linking rather than collagen synthesis (see column 5, lines 30-33). The reference teaches that wounds may heal with large, raised collagenous scars known as keloids or hypertrophic scars. Both keloids and hypertrophic scars are

characterized by excessive collagen deposition, the causes remain obscure (see column 8, lines 63-64). Furthermore, the reference indicates that keloid and hypertrophic scar formation is unique to human. Attempts to develop animal models for abnormal scar formation have always proved unsuccessful (see column 9, lines 19-22). Additionally, the reference teaches that no known circulating stimulatory factor, immune or otherwise, that could account for excessive collagen production in keloids, has been documented (see column 9, lines 49-51). The reference indicates that although the fibroblast provides the forces for contraction, the connective tissue matrix present within the area of tissue repair also plays an important role in the contractile process; one can conclude that, although the active process of contraction is not altered by inhibiting collagen synthesis or deposition, collagen provide the strength and integrity to maintain contracture once it has occurred (see column 4, lines 2-9).

The art provide guidance as to how to treat dermatological disorders such as hypertrophic scars, keloids, dermatofibroms and reduce the symptoms of these diseases, but do not provide guidance as how to how to determine individuals who are susceptible to these diseases, and it is unclear from the prior arts, which proteins or cells are involved in the process.

(3) The relative skill of those in the art:

The relative skill of those in the art is high.

(6) The amount of direction or guidance presented and (7) The presence or absence of working examples:

Example 1 provides dose-dependent inhibition of DNA synthesis of human fibroblast cells in vitro (see Figure 3). Human fibroblast cells were incubated with the inhibitors (Actinonin and Lys[Z(NO_2)]thiazolidide)). ^{3}[H]-Methylthymidine was added to the culture medium, and the amount of the radioactive incorporated into the DNA was measured after 6 hours (see Example 1). The working example provides guidance as how to "decrease" DNA synthesis of fibroblast dose-dependently, but do not provide guidance as how to prevent dermatologic diseases such hypertrophic scars, keloids, dermatofibroms from occurring, the patient population, and when the inhibitor combinations should be administered.

As described above, the Merck manual indicates that keloids are smooth overgrowth of fibroblastic tissue that arise in an area of injury or, occasionally, spontaneously. The Merck manual indicates that keloidal scar tissue always extends beyond the area of original injury. Furthermore, the Merck manual indicates that diagnosis is clinical and treatment is often ineffective. Surgical or laser excision may debulk lesions, but they often recur (see Merck manual, "Keloids").

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boundaries of the initial boundaries of the initial injury and may undergo partial spontaneous resolution, and are common after thermal injuries and other injuries that involve the deep dermis (see Background). The reference indicates that as scar matures, the tensile strength of the scar improves as a result of progressive cross-linking collagen fibers. Furthermore, the reference indicates that Kischer and Brody declared the collagen nodule to be the identifying structural unit of hypertrophic scars and keloids; the nodule, which is absent from mature scars, contains a high density of fibroblasts and unidirectional collagen fibrils in a highly organized and distinct orientation. The reference indicates that the most consistent difference between hypertrophic scar and keloids is the presence of broad, dull, pink bundles of collagen in keloids, which are not present in hypertrophic scars (see Pathophysiology). Furthermore, the reference indicates that keloids and hypertrophic scars do not usually cause symptoms, but they may be tender, painful, or pruritic or they may cause a burning sensation (see History). The reference indicates that the exact mechanisms of keloids and hypertrophic scar pathogenesis is known, and no specific gene or set of genes has been identified; the presence of foreign material, infection, hematoma, or increased skin tension can also lead to keloid or hypertrophic scar formation in susceptible individuals (see Causes). Further, formation of collagen in keloids and hypertrophic scars in the inflammatory stage takes much longer than usual in healing wounds. Collagen fibers in granulation tissue are arranged in a whorled pattern; in keloids, the nodules demonstrate thick, hyalinized bands in the central portion of the nodule (see Histologic Findings). The reference indicates that “prevention is key", and

indicates that preventive measures are: 1) avoid performing nonessential cosmetic surgery, 2) close all surgical wounds with minimal tension, 3) incisions should not cross joint spaces, and 4) avoid making midchest incisions (see Medical care). The reference describes different types of treatments and therapies (see Medical care and Surgical care).

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Young et al (US Patent No. 5,827,735) teaches that degradation of collagen is as important as collagen production and lack of collagen degradation can result in excessive deposition, i.e., keloid, hypertrophic scar, or hepatic fibrosis (see column 5,

lines 11-18). Furthermore, the reference teaches that it is important to note that collagen synthesis has nothing to do with the gain in wound tensile strength. Tensile strength results from collagen cross-linking rather than collagen synthesis (see column 5, lines 30-33). The reference teaches that wounds may heal with large, raised collagenous scars known as keloids or hypertrophic scars. Both keloids and hypertrophic scars are characterized by excessive collagen deposition, the causes remain obscure (see column 8, lines 63-64). Furthermore, the reference indicates that keloid and hypertrophic scar formation is unique to human. Attempts to develop animal models for abnormal scar formation have always proved unsuccessful (see column 9, lines 19-22). Additionally, the reference teaches that no known circulating stimulatory factor, immune or otherwise, that could account for excessive collagen production in keloids, has been documented (see column 9, lines 49-51). The reference indicates that although the fibroblast provides the forces for contraction, the connective tissue matrix present within the area of tissue repair also plays an important role in the contractile process; one can conclude that, although the active process of contraction is not altered by inhibiting collagen synthesis or deposition, collagen provide the strength and integrity to maintain contracture once it has occurred (see column 4, lines 2-9).

However, the claims are not enabled because the specification represent insufficient guidance and objective evidence to predictably enable the use of the claimed invention. As described in Young patent '735, keloid and hypertrophic scar formation is unique to human. Attempts to develop animal models for abnormal scar formation have always proved unsuccessful (see column 9, lines 19-22). Furthermore,

the prior arts indicate that the lack of collagen degradation (collagen crosslinking) result in excessive deposition, i.e., keloid, hypertrophic scar, or hepatic fibrosis. Thus, the claims are not enabled for prevention of dermatological diseases including a hyperproliferation and changed differentiation states of fibroblasts (including benign fibrotic and sclerotic diseases such as hypertrophic scars, keloids, dermatofibroms). Additionally, other cells involved in wound healing, such as keratinocytes secrete collagens (see The Journal of Investigative Dermatology, 1985, 85(1): 79-81). Therefore, the claims are not enabled for the prevention of benign fibrotic and sclerotic diseases by inhibition of DNA synthesis of human fibroblasts, since the prior arts indicate collagen is involved in scar formation such as in keloids, hypertrophic scars, and TNF-β involvement in dermatofibroms. Therefore, by inhibiting DNA synthesis of fibroblast would not treat or prevent the occurrences of keloid, hypertrophic scars, dermatofibroms or other benign fibrotic and sclerotic diseases.

The art provide guidance as to how to treat certain dermatologic diseases and conditions, and the progression of symptoms of these dermatologic diseases, but do not provide guidance as how to how to determine individuals who are susceptible to damages and dermatologic diseases and other disorders, and when the pharmaceutical composition should be administered for prevention of such diseases or disorders.

(8) The quantity of experimentation necessary:

Since it is uncertain to predict the patient population who are susceptible for dermatologic diseases, alopecia, and other diseases such as cancer, and the Applicant

have not provided the appropriate time frame at which the compound should be administered, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine if the inhibitors of DP IV and APN would be effective in preventing dermatologic diseases, including cancer. In view of the teachings above, and the lack of guidance and or exemplification in the specification, it would not be predictable that the method would function as contemplated. Thus, it would require undue experimentation by one of skill in the art to practice the invention as claimed.

Please note that the term "prevent" in an absolute definition which means to stop from occurring and, thus, requires a higher standard for enablement than does "therapeutic" or "treat" or "alleviate", especially since it is notoriously well accepted in the medical art that the vast majority of afflictions/disorders suffered by mankind cannot be totally prevented with current therapies (other than certain vaccination regimes)-including preventing such disorders as dermatologic diseases including cancer and alopecia, which is clearly not recognized in the medical art.

12. Claims 5 and 13-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008,

1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the

sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a method utilizing the inhibitor combinations (DP IV and their analogs, inhibitors of APN and their analogs and derivatives of dipeptide, side chain protected derivatives and their derivatives that serve as the amide structure) for a prevention and therapy of dermatological diseases. The generic statements DP IV analogs, APN analogs, derivatives of dipeptide, side chain protected derivatives, derivatives that serve as the amide structure, and APN inhibitor derivatives do not provide ample written description for the compounds since the claims do not describe a single structural feature. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claims 5, 13-14 are broad generics with respect all possible compounds

encompassed by the claims. The possible structural variations are limitless to any class of peptide or a peptide-like molecule that can form peptide bonds and make up the class of DP IV analogs, APN analogs, and their derivatives. It must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives. The specification is void of organic molecules that functions as a peptide-like molecule that qualify for the functional characteristics claimed as a peptide or a peptide-like molecule or other peptidic molecules, and other synthetic peptide or peptide-like molecule that can function as proteases.

The specification is limited to the Lys[Z(NO_2)]thiazolidide (I49) and phosphonic acid diaryl ester (I63), dipeptide boronic acids and their salts, Xaa-Xaa-(Trp)-Pro-(Xaa)n peptides and amino acid-(Xaa) amides for DP IV inhibitors and actinonin, bestatin, probestin, phebestin, RB3014 or leuhistin for APN inhibitor (see paragraphs [0012]-[0013]). The specification discloses that the preferred effectors for DP IV are for example Xaa-Pro dipeptides, corresponding derivatives and their salts (see paragraph

[0012]). The specification discloses that the preferred inhibitors of APN are bestatin (Ubenimex), actinonin, probestine, phebestine, RB3014 or leuhistine (see paragraph [0013]). The working example describe the dose-dependent inhibition of DNA synthesis of I49 (DP IV inhibitor) and actinonin (APN inhibitor) on human fibroblast cells in vitro (see Example 1). The specification does not describe any other inhibitors of DP IV, such as dipeptide derivatives and Xaa-Xaa-(Trp)-Pro-(Xaa)n derivatives that would encompass the derivatives and variants of Xaa-Pro dipeptide derivatives. Descriptions I63, Xaa-Pro and Lys[Z(NO_2)]thiazolidide (I49) for DP IV inhibitors and bestatin (Ubenimex), actinonine, probestine, phebestine, RB3014 or leuhistine for APN inhibitors are not sufficient to encompass numerous other proteins and derivatives that belong to the same genus. For example, there are varying lengths, varying amino acid compositions, and numerous distinct qualities that make up the genus. There are 20 naturally occurring amino acids that can be used as Xaa. Additionally, there are non-naturally occurring amino acids, such as D-amino acids, and amino acid mimetics or peptidomimetics, and other modified amino acids that can be substituted for Xaa to increase the number of possibilities. Furthermore, Xaa-Xaa-(Trp)-Pro-(Xaa)n peptides and their corresponding derivatives and salts would have vast number of possibilities, since n can be 0 to 10. Since there are 20 naturally occurring, and D-isomers and amino acids mimetics or peptide mimetics and other modified amino acids, the peptides and derivatives are innumerable. There would be at least 20 different possibilities for the first Xaa, and at least 20 different possibilities for the 2nd Xaa and at least 20 amino acid possibilities for the 3rd Xaa. Since the 3rd Xaa can be 0 to 10 amino acids, this further

increase the numbers of possibilities for this peptide alone. Furthermore, side chain protected derivatives could be anything, even a side chain that has been modified with an amino acid or an alkyl group. Therefore, the numbers of possibilities are innumerable. Additionally, α-aminophosphinic acid derivatives would further increase the APN inhibitor derivative possibilities since the derivatives can be anything, and the limits (types of modification, variance and homologous) are not provided in the specification. Therefore, there is not sufficient amount of examples provided to encompass the numerous characteristics of the whole genus claimed.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Rejection-35 U.S.C. 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 5 and 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Ansorge (WO 02/053170 (published July 11, 2002), machine translation used).

The instant claim is drawn to a method utilizing the inhibitor combinations (DPIV inhibitor and APN inhibitor) for a prevention of benign fibrotic and sclerotic diseases.

Ansorge et al teach the combined used of DP IV inhibitor (Lys[Z(NO_2)]thiazolidide) and APN inhibitor (actinonin) for the treatment of atherosclerosis and dermatological diseases (see paragraph 5 of the translated document). Furthermore, the reference teaches simultaneous administration of inhibitors and the administration is as topical application in the fore of creams, ointments, pastes, gels, solutions, spray, liposomes and systemic application to the oral, transdermal, intravenous, subcutaneous, intracutaneous, intramuscular with pharmaceutically acceptable carrier (see paragraphs 6 and 9 of the translated document). Since the elected compound is taught by the reference and is disclosed that the compound can be used to treat dermatological diseases, this meets the limitation of claims 5 and 13-14. The claims are drawn to a method of preventing dermatological diseases (benign fibrotic and sclerotic diseases). Since prevention implies future events, by virtue of administering the combination of DP IV inhibitor (Lys[Z(NO_2)]thiazolidide) and APN inhibitor (actinonin) to a patient, implies dermatological diseases are prevented. Anybody, including patients suffering from hypertrophic scars, keloids, and other post-infection and post-traumatic conditions can suffer from dermatologic diseases. Therefore, since Ansorge reference teaches the use of DP IV inhibitor

(Lys[Z(NO_2)]thiazolidide) and APN inhibitor (actinonin) to treat atherosclerosis and other dermatological diseases, this administration would prevent hypertrophic scars, keloids, dermatofibroms and other benign fibrotic and sclerotic diseases in the same patients administered the combination. Therefore, the reference meets the limitations of claims 5 and 13-14.

Conclusion

15. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Julie Ha/
Examiner, Art Unit 1654

/Anish Gupta/
Primary Examiner, Art Unit 1654